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# Analyses of the cost-effectiveness of pooled alendronate and risedronate, compared with strontium ranelate, raloxifene, etidronate and teriparatide

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## Executive Summary

This report focuses on the cost-effectiveness of interventions for the treatment of osteoporosis. Where this report differs from those previously published is that it explicitly takes the costs of opportunistic assessment of women whilst attending their GP clinic for another topic and the costs of BMD scanning into account.
This is of great importance as previous guidance may have specified T-Score thresholds at which treatment is cost-effective, but excluded the costs of ascertaining this information.
Our results suggest that it may be cost-effective to opportunistically assess all women aged 70 years or over attending a GP clinic, with BMD scans being offered to all women bar those aged 70 –74 years with no clinical risk factors. T-Scores thresholds at which it could be cost-effective to treat combinations of age and clinical risk factors are provided in the text.
For women who present with a self-identifying risk factor (an acute fracture, rheumatoid arthritis or taken high doses of glucocorticoids) it may be cost-effective to offer BMD scans to selected women aged 55 years and over. The number of clinical risk factors required to be offered a BMD scan, and the T-Score threshold required for treatment to be considered cost-effective is provided in the text.

The results are largely influenced by the price of interventions and it is likely that the price of alendronate will decrease following the launch of a generic. Some sensitivity analyses have been conducted on price, however it may be that these results need to be revised once the timing of the reduction and the exact reduction is known.

Other considerations that change the age band at which opportunistic assessment strategies and BMD scanning strategies are cost-effective are the relative risk of treatment on risk factors other than low BMD and prior fracture status; the assumed disutility of a vertebral fracture in the year of fracture; the persistence of women with treatment and the disutility associated with treatment.

## 1. Introduction.

After the Appraisal Committee discussed the cost-effectiveness results for osteoporosis drugs at their meeting in November 2005, [1] it asked for a number of additional scenarios to be analysed. A key component of the additional work was to estimate the likely costs and disutilities associated with side effects relating to bisphosphonate treatment. A literature search has been undertaken, [2] with only summarised data presented in this report.

Additional sensitivity analyses have been undertaken on the level of persistence, the assumed efficacy of bisphosphonates in women whose absolute risk of fracture is driven by risk factors for fractures other than low bone mineral density (BMD) or previous fracture, the costs of fracture, the disutility of vertebral fracture in the initial year and the acquisition cost of bisphosphonates

## 2. Modelling Methodology.

The modelling methodology is very similar to that previously used and focuses on women with T-Scores of <1 and > -5.5 SD. 1 On the request of the Committee [3] T-Scores have been grouped into bands of 0.5SD with the midpoint used in the calculations. Thus the T-Score band of -2.5SD to –3.0SD has been calculated using a T-Score of –2.75SD, with the results assumed applicable to all T-Scores in this band. In this report, results are expressed as the upper bound of the relevant T-score band. This reflects that fact the results apply to all women within the T-score band, i.e. all women whose T-scores are below the upper bound. For example if treatment is considered to become cost-effective for the above group, we would report an intervention threshold of < -2.5SD.

The gradation level of 0.5SD is much larger than that of 0.1SD used in the previous report [1] with a corresponding risk of greater error. For example, the possibility for different treatment decisions for women with T-Scores of –2.44 SD and -2.51SD is larger where these are allocated into T-score bands of 0.5SD in width (i.e. T-score band with upper bound of -2.0 for the first woman and -2.5 for the second woman) than in a methodology which rounds these to –2.4 SD and –2.5SD respectively. This increased error is not however associated with any known systematic bias.

Additionally, on the request of the committee, the efficacy data from risedronate and alendronate, the bisphosphonates with the greatest randomised controlled trial data have been pooled and the average price assumed within the analyses.

Furthermore it was requested that the results for women aged 80 years and over would be assumed equal to those women aged 75-79 years.

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[1] http://www.nice.org.uk/page.aspx?o=273846

[2] Adverse effects and persistence with therapy in patients taking oral alendronate, etidronate or risedronate: a systematic review. Lloyd Jones M, Wilkinson A. ScHARR, University of Sheffield 2006.

[3] http://www.nice.org.uk/page.aspx?o=305735

The base-case scenario includes costs and disutilities associated with bisphosphonate use. These have been calculated as described below. Refer to the accompanying document for a fuller report on the side-effects and persistence levels of bisphosphonates.

1) Bisphosphonates are associated with an increased risk of upper gastro-intestinal (GI) problems that will require a GP consultation. The rate of this (over and above a background level of average women) is assumed to be 23.5 GP consultations per 1,000 patient months in the initial treatment month, and 3.5 GP consultations per 1,000 patient months in subsequent months taken from the most appropriate study identified in the systematic literature review. The additional number of GP consultations per month for patients on bisphosphonate treatment has been calculated assuming that patients have an average level of dyspepsia. Data from Van Staa et al [4] have shown that GI problems are more prevalent in patients suffering osteoporosis, and that there is only a slight increase in GI problems for those patients taking etidronate (an early bisphosphonate). As such our results may be unfavourable to the bisphosphonate.
2) A GP consultation is assumed to cost £18, and a course of H2 receptor antagonists, or equivalent is assumed to cost £1.50, totalling £19.50 per GP visit. The price of the H2 receptor antagonist is approximately 1 month at high dose or 2 months at low dose. It is assumed that were the patient to receive an additional course of treatment this would be associated with an additional GP consultation. The base-case assumes that H2 receptor antagonists are prescribed. If proton pump inhibitors (PPI) were used instead of H2 receptor antagonist, the costs of the interventions used to treat dyspepsia would rise with the average cost of PPI treatment for one month being approximately £20 taking into account different drug formulations and branded and generic types.
3) The utility loss associated with GI problems that require a GP consultation has been assumed to replicate "abdominal symptoms once a day that is not always resolved with medication, certain foods, drinks and pain relievers may need to be avoided, wake up in the night once a week, and often feel anxious". This has a time trade off value of 0.91 in Groeneveld et al. [5] These symptoms are assumed to last a full month. This assumption has been made deliberately pessimistic towards the intervention and will increase the cost per QALY of intervention. This was assumed as GI problems that do not require a GP consultation and other conditions, such as nausea that may well be associated with bisphosphonate use but where background rates are not known, have been excluded from the analysis, and would otherwise have under-estimated the cost per QALY of an intervention.
4) That the long-term compliance with bisphosphonates is 50%. We have assumed, that 50% of patients complete the full 5-year course. It is assumed that the remaining 50% receive 3 months of drug treatment for no health gain.

[4] van Staa, T., Abenhaim, L., and Cooper, C. Upper gastrointestinal adverse events and cyclical etidronate. *American Journal of Medicine* 1997; 103 462-467.
[5] Groeneveld PW, Lieu TA, Fendrick M, Hurley LB, Ackerson LM, Levin TR and Allison JE. "Quality of life measurements clarifies the cost-effectiveness of Helicobacter Pylori eradication in peptic ulcer disease and uninvestigated dyspepsia" The American Journal of Gastroenterology. 2001 96 (2) 338 - 347

Three months of treatment is assumed to be an approximate weighted average, with some patients stopping after 1 month. Whilst some fulfilling their prescription for a longer period whilst not being persistent. In reality those women that discontinue treatment are likely to do so at time points throughout the 5-year period and will receive some health benefit and additional drug costs. These however are difficult to model and are excluded from the model.

5) The mathematical model used calculates the costs and QALYs per 100 patients who complete the full 5-year treatment period. In the initial month of treatment 200 patients will be need to be treated as compliance has been assumed to be 50%. This will require an extra 4.7 GP consultations (23.5*200/1000) in the month of initiation. After the first month only an additional 0.35 GP consultations will be required (3.5*100/1000) per month. These costs when discounted at 6% per annum, approximately totals £4.50 per treated patient over the 5-year period where patients are assumed to be treated with H2 receptor antagonists. If PPIs were prescribed this cost rises to £8.78 per treated patient.
6) The QALYs lost per patient treated over the 5-year period is dependent on age as we assume a multiplier effect (0.91 from Groenveld et al ) on the average utility for GI symptoms. Thus patients who are younger and have a higher starting utility will have a greater disutility. The average QALY losses per patient over the 5-year period range from 0.0013 QALY at age 75 to 0.0016 at 50 years of age. Benefits have been discounted at 1.5% per annum. We have not adjusted the QALY losses of GI symptoms when a patient's utility has been reduced following a fracture, as such the cost per QALY may be slightly overestimated.

The base-case scenario

The base-case is assumed to be that described in Table 1.

Table 1: The base-case scenario.

| Parameter | Value | Source |
|---|---|---|
| Persistence at 5-years | 50% | Estimated from the results of the accompanying literature review |
| The assumed relative risk of bisphosphonates on osteoporotic fractures. | 0.71 – 'hip'<br>0.58 – 'spine'<br>0.78 – 'prox hum'<br>0.78 – 'wrist' | Systematic Review and meta-analysis of alendronate and risedronate data. See Appendix 1. |
| Costs set to those used in the initial report | Age dependent, see previous report | Updated costs used in previous NICE assessments of osteoporosis interventions. |
| Utility multiplier associated with vertebral fracture. | Year 1 0.626<br>Year 2+ 0.909 | Kanis et al. *Osteoporosis International* 2004; 15 20-26. This source was used for all fracture types |
| Costs incurred over 5-years via side effects associated with bisphosphonate | £4.50 per patient that is compliant (costs for non-compliant patients are included in our analyses) | See earlier text |
| Utility multiplier associated with bisphosphonate related GI symptoms | 0.91<br>(utility losses for non-compliant patients are included in our analyses) | Groenveld et al [6] |
| Cost of bisphosphonate | £264 per annum | Mean price of alendronate and risedronate.[7] |

[6] Groeneveld PW, Lieu TA, Fendrick M, Hurley LB, Ackerson LM, Levin TR and Allison JE. "Quality of life measurements clarifies the cost-effectiveness of Helicobacter Pylori eradication in peptic ulcer disease and uninvestigated dyspepsia" The American Journal of Gastroenterology. 2001 96 (2) 338 - 347

[7] Taken from http://www.bnf.org/bnf/ BNF 51. Accessed 01/07/06.

Sensitivity Analyses undertaken.

The sensitivity analyses undertaken for bisphosphonates are given in Table 2. All other parameters are held at their base-case values. One exception will be where persistence is changed which will have slight impacts on the side-effect values as fewer or more people will need to be treated in month 1 to achieve the 100 successfully treated women over the 5-year period that is the base unit of the model.

Table 2: Sensitivity analyses

| | Parameter to be changed | Value for sensitivity analysis | Rationale |
|---|---|---|---|
| 1 | Persistence | 25% | General uncertainty on the expected level persistence. |
| 2 | Persistence | 75% | General uncertainty on the expected level persistence. |
| 3 | Efficacy (relative risk) on fractures associated with low BMD, previous fractures, steroid use, parental history of fracture, rheumatoid arthritis, smoking and alcohol consumption | T-Score <-2.5 SD<br>0.44 – 'hip', 0.50 – 'spine',<br>0.64 – 'prox hum', 0.64 – 'wrist'<br><br>T-Score <-2.0 SD and >-2.5 SD<br>1.84 – 'hip', 0.54 – 'spine',<br>1.03 – 'prox hum', 1.03 – 'wrist'<br><br>T-Score >-2.0 SD<br>1.84 – 'hip', 0.82 – 'spine',<br>1.14 – 'prox hum', 1.14 – 'wrist' | Hypothesis that osteoporosis drugs are more efficacious in patients with lower BMD values.<br><br>Sub-group analyses taken from the FIT trial. [8] |
| 4 | Efficacy on fractures associated with steroid use, parental history of fracture, rheumatoid arthritis, smoking and alcohol consumption | 0.86 – 'hip'<br>0.79 – 'spine'<br>0.89 – 'prox hum'<br>0.89 – 'wrist' | Hypothesis that the efficacy of osteoporosis drugs is only proven in patients with low BMD or with a prior fracture. |
| 5 | Efficacy on fractures associated with steroid use, parental history of fracture, rheumatoid arthritis, smoking and alcohol consumption | 1.00 – 'hip'<br>1.00 – 'spine'<br>1.00 – 'prox hum'<br>1.00 – 'wrist' | Hypothesis that the efficacy of osteoporosis drugs is only proven in patients with low BMD or with a prior fracture. |
| 6 | Fracture Costs | Set to those of Stevenson et al. Women's Health Medicine (In Press) with additional costs added for home help requirements. | New data have emerged since the earlier report was completed. See Appendix 2 |

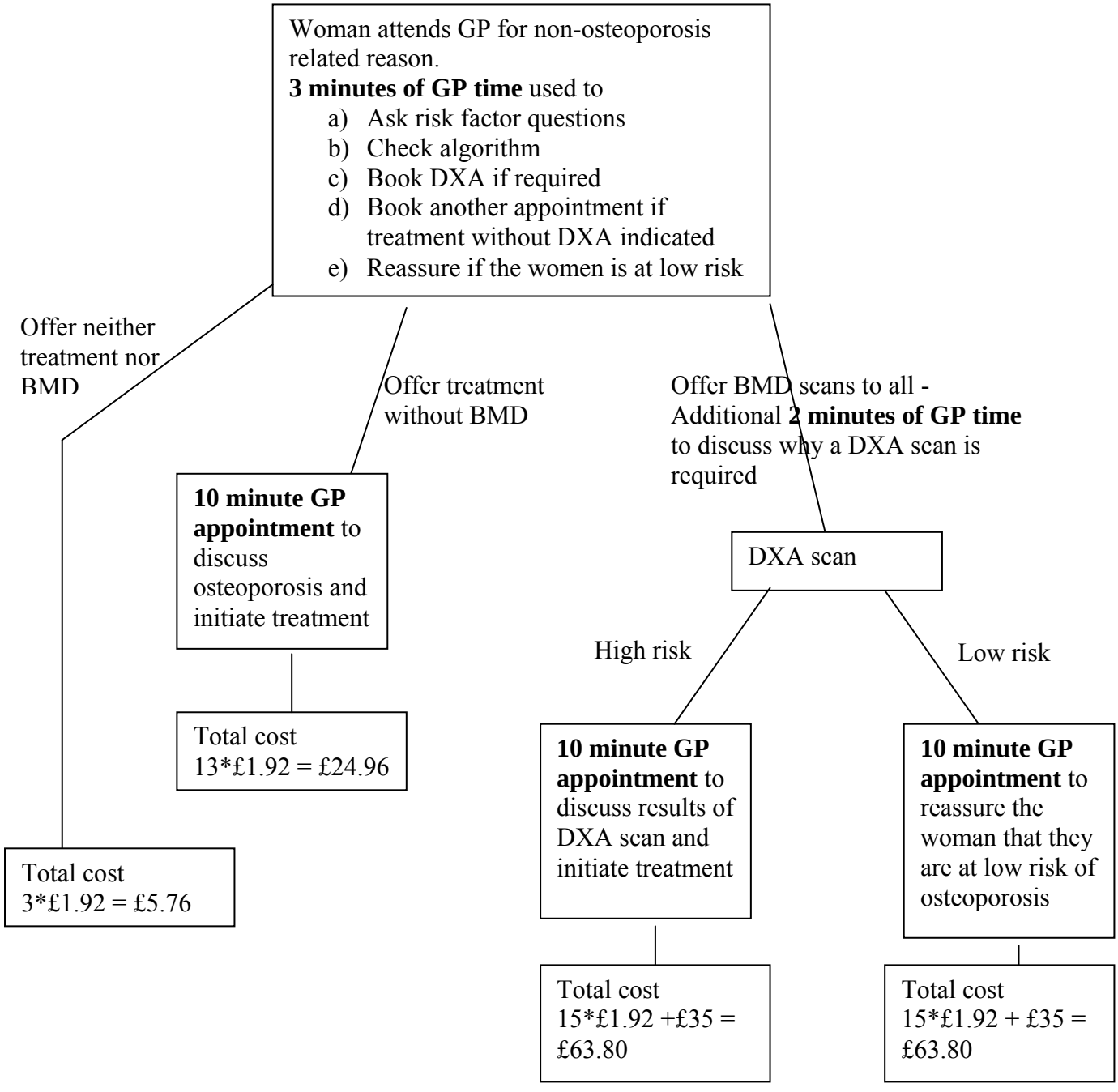
[8] Cummings S et al. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: results from the Fracture Intervention Trial. JAMA 1998, 280(24): 2077-82

| | | | |
|---|---|---|---|
| 7 | Fracture Costs | Age dependent. Set to those of Stevenson et al. Women's Health Medicine (In Press). | New data have emerged since the earlier report was completed. See Appendix 2 |
| 8 | Fracture Costs | Age dependent. Set to the nearest Health Resource Group, with additional costs added for home help requirements. | HRG groups have emerged since the completion of the earlier report. See Appendix 2 |
| 9 | Fracture Costs | Set to the nearest Health Resource Group. | HRG groups have emerged since the completion of the earlier report. See Appendix 2 |
| 10 | Utility multiplier associated with vertebral fracture. | Set to the value for hip in year 1. 0.792 | Committee's belief that vertebral fracture will not produce higher disutility in year 1 than a hip fracture |
| 11 | Costs and disutility incurred over 5-years via side effects associated with bisphosphonates. Base-case assumptions doubled. | £9.00 per patient that is compliant. Utility multiplier of 0.82 associated with bisphosphonate related GI symptoms (costs and disutilities for non-compliant patients have been included) | General uncertainty on the costs and disutilities of bisphosphonate side effects. |
| 12 | Disutility incurred over 5-years via side effects associated with bisphosphonates. Base-case assumptions halved | £2.25 per patient that is compliant. Utility multiplier of 0.955 associated with bisphosphonate related GI symptoms (costs and disutilities for non-compliant patients have been included) | General uncertainty on the costs and disutilities of bisphosphonate side effects. |
| 13 | Disutility incurred over 5-years via side effects associated with bisphosphonate | No costs or disutilities assumed | General uncertainty on the costs and disutilities of bisphosphonate side effects. |
| 14 | Disutility incurred over 5-years via side effects associated with bisphosphonates. 10 x base-case disutility assumption. | Utility multiplier of 0.10 associated with bisphosphonate related GI symptoms. (disutilities for non-compliant patients have been included) | General uncertainty on the disutilities of bisphosphonate side effects. |
| 15 | Costs incurred over 5-years via side effects associated with bisphosphonate | Cost of £8.78 per patient that is compliant (costs for non-compliant patients have been included) | Increase in costs if proton pump inhibitors were prescribed for dyspepsia rather than H2 receptor antagonists. |
| 16 | Cost of bisphosphonate | £132 per annum | Costs halved in expectation of generic alendronate in the near future. (Prior to 2007) |

Each scenario has been analysed for two distinct groups of women. Once for those women who are opportunistically questioned by the GP during a consultation on a separate topic (annotated as '1' in section 3.2), and once for women who have sustained an acute fracture, have rheumatoid arthritis or are on high dose glucocorticoids (i.e. who present with a self-identifying risk factor) and who do not have to be identified from amongst the general populous (annotated as '2' in section 3.2).

The assumed costs of opportunistically assessing women during a GP visit.

For women who are opportunistically questioned about their risk factors the following algorithm has been used to determine the quantity of GP time required.



Following initiation of treatment it was assumed, on advice from the NICE GDG that as there are requirements to review all medications in the elderly, for women over the age of 75 years the review of osteoporosis medication would be done during the same consultation and a marginal cost of zero was applied. For women under 75 years of age, the GPs on the NICEGDG estimated that 2/3 of the population would already be on long-term medication, and thus that only 1/3 of the population would be reviewed annually by a GP, each incurring a cost of £18.

Analyses for women who present with a self-identifying risk factor.

For patients who do not have to be identified from the general populous, it has been assumed that assessment of other risk factors will occur at the same time as the consultation booked because of the self-identifying risk factor (for example acute fracture or rheumatoid arthritis). Where BMD scanning is considered cost-effective (see results section), the scan has been included at a cost of £35, together with 1 GP appointment to discuss the results of the BMD scan and initiation of treatment where appropriate.

Calculating cost per QALY ratios.

For the purposes of cost-effectiveness analyses, a cost per QALY threshold of £20,000 has been used. On the request of the committee the results at age 75-79 years are assumed applicable for women aged 80 years and older.

For women who will be opportunistically questioned the cost per QALY of treatment with bisphosphonates versus no treatment were calculated for all combinations of risk factors (bar a prior fracture) . In order to simplify the results only the median cost per QALY was used for women with one, two or three or more clinical risk factors.

For women who present with a self-identifying risk factor (for example acute fracture or rheumatoid arthritis), the increased in risk of fracture associated with a prior fracture was assumed applicable to all patients, providing one cost per QALY value.

For each age band, the following calculations were undertaken to see whether opportunistic assessment, BMD scanning and treatment were cost effective. It was assumed that treatment would not be initiated without a BMD scan.

For each combination of number of clinical risk factors and T-Score band, the cost per QALY of treatment compared with no treatment, assuming no identification costs or BMD scanning costs was calculated. Where this was below £20,000 the patient could be cost-effectively treated assuming that their BMD band and number of clinical risk factors were known. For each combination the net benefit of treatment per individual woman (Denoted NBT) was set to zero, if treatment was not cost-effective and thus not provided, and set to 20,000 * the incremental QALYs per woman due to treatment minus the incremental cost of treatment per woman, where treatment was cost-effective.

The individual NBT are multiplied by the number of women in clinical risk factor group and summated to find a total net benefit of treatment for the clinical risk factor group.

The costs of BMD scanning all the women within this clinical risk factor group was subtracted, this value being denoted NBS. If NBS is greater than 0, then BMD scanning for all women in the clinical risk factor category is cost-effective given that the number of risk factors was known. Conversely, where NBS is equal or lower than 0 then BMD scanning should not be employed for women within this clinical risk factor group. Values of NBS below 0 were set to zero, as no BMD scanning would be performed at this level of clinical risk factors.

For women with an identifying risk factor, it is assumed that information about the number of clinical risk factors is obtained without cost, and where BMD scanning is considered cost-effective for women of a certain age and with a number of clinical risk factors then this should be undertaken. The decision whether to treat or not, would be decided on whether the patient had reached an appropriate T-Score threshold, defined as one where the net benefit of treatment was greater than zero.

However for patients who are opportunistically questioned there is a cost associated with determining the number of clinical risk factors a woman has. To determine whether assessing the women is considered cost-effective, the costs of opportunistically assessing all women in this age band is subtracted from the summation of the NBS value for the clinical risk factor groups. This value is denoted NBQ.

Where NBQ is positive then opportunistically assessing women is considered cost-effective. Women at this age should be questioned, receive a BMD scan where appropriate, and treated where the appropriate T-Score threshold is reached. Conversely, where NBQ is equal or less than zero, opportunistically assessing women is not cost-effective, as the costs of this are greater than the gains accrued from the women who could be cost-effectively treated.

In formal notation this is.

For each age group the following calculations are performed.

$_i$ = 1 to 13, for each of the 13 T-Score bands from >-5.5 SD to <1.0 SD in blocks of 0.5 SD

$_j$ = 0 to 3, for each of the number of clinical risk factors a women may have.

$\Delta Q_{ij}$ = QALY gain expected through treatment for 1 woman of T-Score $_i$ and clinical risk factor $_j$

$\Delta C_{ij}$ = Cost increase expected through treatment for 1 woman of T-Score $_i$ and clinical risk factor $_j$

$NBT_{ij} = \max (\Delta Q_{ij} * £20{,}000 - \Delta C_{ij}, 0)$

For each j

$NBS_j = \Sigma (_i = 1 \text{ to } 13)$ (NBT $_{ij}$ * Number of women ij) – Cost of BMD Scan * Number of women $_j$

For women presenting with an acute fracture, with rheumatoid arthritis or being initiated on high dose gluco-corticoids. It is assumed that the number of clinical risk factors are known and thus.

Where $NBS_j > 0$ BMD scanning is cost-effective, BMD all women in this clinical risk factor group and treat where $NBT_{ij} > 0$

Where $NBS_j <= 0$ BMD scanning is not cost-effective for women in this clinical risk factor group.

For women who are opportunistically questioned.

$NBQ = \Sigma (_j = 0 \text{ to } 3)$ (max ($NBS_j$, 0) – Cost of opportunistic assessment * Number of women

Where $NBQ > 0$ opportunistically assessing women is cost-effective. BMD where $NBS_j > 0$ and treat where $NBT_{ij} > 0$

Where $NBQ < 0$ opportunistically assessing women is not a cost-effective strategy.

## 3. Results for pooled alendronate and risedronate

### 3.1 The base-case results and the impact of the assumptions for all sensitivity analyses.

*Primary Prevention (i.e. women identified through opportunistic assessment)*

| | How scenario is different from the base-case. | Identification strategies potentially[9] cost-effective from what age (years)? | Percentage of women age 50 or older that were opportunistically assessed that would be offered a BMD scan (%) $^{\nabla}$ | Percentage of women age 50 or older that were opportunistically assessed that would be treated (%) $^{\nabla\psi}$ |
|---|---|---|---|---|
| Base-case | - | 70 | 25.7 | 2.5 |
| 1 | Persistence set to 25% | 70 | 9.2 | 0.7 |
| 2 | Persistence set to 75% | 70 | 25.7 | 3.8 |
| 3 | Efficacy assumed to be different in the osteoporotic, osteopenic and normal women, and equal to that from the FIT trial. | 65 | 38.5 | 4.6 |
| 4 | Efficacy of bisphosphonate set to 50% for clinical risk factor other than BMD and fracture status. | 75 | 5.7 | 0.6 |
| 5 | Efficacy of bisphosphonate set to 0% for clinical risk factor other than BMD and fracture status. $^{\blacklozenge}$ | N/A | - | - |
| 6 | The costs calculated by Stevenson et al [10] to be used instead of the older costs, including potential home help costs. | 70 | 25.7 | 2.6 |
| 7 | The costs calculated by Stevenson et al to be used instead of the older costs, excluded potential home help costs. | 70 | 25.7 | 2.5 |
| 8 | HRG costs to be used, including potential home help costs. | 70 | 25.7 | 2.5 |
| 9 | HRG costs to be used, excluding potential home help costs. | 70 | 9.2 | 1.3 |
| 10 | Vertebral disutility to be set to equal that associated with a hip fracture. | 70 | 9.2 | 0.9 |
| 11 | The costs and disutility from side effects to be double that estimated | 70 | 25.7 | 2.5 |
| 12 | The costs and disutility from side effects to be half that estimated | 70 | 25.7 | 2.5 |
| 13 | The costs and disutility from side effects to be set to zero | 70 | 25.7 | 2.5 |
| 14 | The disutility from side effects to be set to ten times that of the base-case | 70 | 9.2 | 0.8 |
| 15 | The costs from side effects increased were proton pump inhibitors are prescribed instead of H2 receptor antagonists. | 70 | 25.7 | 2.5 |
| 16 | The costs of bisphosphonates halved. | 65 | 34.8 | 8.2 |

[9] Assuming a cost per QALY of £20,000

[10] Stevenson MD, Davis SE, Kanis JA. "The hospitalisation costs and out-patient costs of fragility fractures". Women's Health Medicine. In Press.

▽ These are the BMD Scans and people treated assuming that all women were opportunistically screened immediately. Once this had been achieved, the numbers will be significantly reduced, assuming that opportunistic assessment of clinical risk factors would be undertaken once every 5 years, and that people on treatment would not be re-assessed.

Ψ These numbers have taken persistence into account. Thus, where persistence is 50%, double this number would be initially offered treatment.

♦ In this instance we assume that GP would not question the woman about their clinical risk profile, with all women at the threshold age or older receiving BMD scans.

*Women with a self- identifying risk factor*

| | How scenario is different from the base-case. | BMD scanning strategies cost-effective from what age (years)? | Percentage of women age 50 or older with a self-identifying risk factor that would be offered a BMD scan (%) [∇] | Percentage of women age 50 or older with a self-identifying risk factor that would be treated (%) [∇Ψ] |
|---|---|---|---|---|
| | - | 55 | 58.2 | 12.6 |
| 1 | Persistence set to 25% | 60 | 54.4 | 5.2 |
| 2 | Persistence set to 75% | 55 | 58.2 | 19.0 |
| 3 | Efficacy assumed to be different in the osteoporotic, osteopenic and normal women, and equal to that from the FIT trial. | 50 | 84.2 | 11.6 |
| 4 | Efficacy of bisphosphonate set to 50% for clinical risk factor other than BMD and fracture status. | 65 | 53.5 | 6.6 |
| 5 | Efficacy of bisphosphonate set to 0% for clinical risk factor other than BMD and fracture status. | 75 | 39.8 | 1.9 |
| 6 | The costs calculated by Stevenson et al to be used instead of the older costs, including potential home help costs. | 55 | 61.7 | 15.5 |
| 7 | The costs calculated by Stevenson et al to be used instead of the older costs, excluded potential home help costs. | 55 | 58.2 | 12.6 |
| 8 | HRG costs to be used, including potential home help costs. | 55 | 58.2 | 12.6 |
| 9 | HRG costs to be used, excluding potential home help costs. | 55 | 58.2 | 11.7 |
| 10 | Vertebral disutility to be set to equal that associated with a hip fracture. | 60 | 57.3 | 10.6 |
| 11 | The costs and disutility from side effects to be double that estimated | 55 | 58.2 | 11.0 |
| 12 | The costs and disutility from side effects to be half that estimated | 55 | 58.2 | 12.6 |
| 13 | The costs and disutility from side effects to be set to zero | 55 | 58.2 | 12.6 |
| 14 | The disutility from side effects to be set to ten times that of the base-case | 60 | 57.3 | 10.6 |
| 15 | The costs from side effects increased were proton pump inhibitors are prescribed instead of H2 receptor antagonists. | 55 | 58.2 | 11.7 |
| 16 | The costs of bisphosphonates halved. | 50 | 75.5 | 26.9 |

[∇] These are the BMD Scans and people treated assuming that all women with a prior fracture were opportunistically screened immediately. Once this had been achieved, the numbers will be significantly reduced, assuming that opportunistic assessment of clinical risk factors would be undertaken once every 5 years, and that people on treatment would not be re-assessed.

[Ψ] These numbers have taken persistence into account. Thus, where persistence is 50%, double this number would be offered treatment.

## 3.2 Detailed analysis for each scenario for women identified through opportunistic assessment

The following matrices give the details for the age-bands where opportunistic assessment strategies are considered cost-effective, whether to refer for BMD scanning, and at what T-Score to initiate treatment for each number of clinical risk factors (0-3) that a woman may have. The final column indicates the overall cost per QALY of an opportunistic screening, BMD and treatment strategy for the age-band, which by definition will be lower than £20,000. For those age bands not included the cost per QALY of an opportunistic screening, BMD and treatment strategy was greater than £20,000.
In these analyses a higher cost per QALY does not necessarily reflect that a strategy is less effective, but could imply that a strategy is more permissive in who is treated. Our methodology (see calculating cost per QALY on page 11) maximises the total net benefit by treating any patient with an individual cost per QALY below £20,000.
For example, if hypothetical scenario A was more favourable to the intervention than hypothetical scenario B, and thus allowed women in an additional T-Score band to be treated, where the cost per QALY was very close to the £20,000 threshold, it is likely that the overall cost per QALY of scenario A would be greater that that for B where women in this T-Score band were not treated and thus the average cost per QALY was lower.

**Scenario Base-case 1**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £14,257 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £12,113 |

**Sensitivity Analysis 1-1: Base-case, bar persistence set to 25%**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £15,928 |
| 75 years and over | Do not BMD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £7,852 |

**Sensitivity Analysis 2-1: Base-case, bar persistence set to 75%**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £13,667 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £11,481 |

**Sensitivity Analysis 3-1: Base-case, bar efficacy assumed to be different in the osteoporotic, osteopenic and normal women, and equal to that from the FIT trial.**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 65-69 years | Do not BMD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | £16,792 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | £12,502 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | £5,726 |

**Sensitivity Analysis 4-1: Base-case, bar efficacy of bisphosphonate set to 50% for clinical risk factor other than BMD and fracture status.**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 75 years and over | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £12,114 |

**Sensitivity Analysis 5-1: Base-case, bar efficacy of bisphosphonate set to 0% for clinical risk factor other than BMD and fracture status. Questions on clinical risk factors are assumed not to be asked.**

Opportunistic assessment strategies have cost per QALYs of >£20,000 at all ages.

**Sensitivity Analysis 6-1: Base-case, bar using the costs calculated by Stevenson et al to be used instead of the older costs, including potential home help costs**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £11,387 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.0 SD | BMD and treat where T-Score <-0.5 SD | £8,501 |

**Sensitivity Analysis 7-1: Base-case, bar using the costs calculated by Stevenson et al to be used instead of the older costs, excluding potential home help costs**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £12,611 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £9,906 |

**Sensitivity Analysis 8-1: Base-case, bar using HRG costs including potential home help costs**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £13,497 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £12,166 |

**Sensitivity Analysis 9-1: Base-case, bar using HRG costs excluding potential home help costs**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £14,965 |
| 75 years and over | Do not BMD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £9,344 |

**Sensitivity Analysis 10-1: Base-case, bar vertebral fracture disutility reduced to that of hip fracture**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | £16,000 |
| 75 years and over | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £6,436 |

**Sensitivity Analysis 11-1: Base-case, bar disutility and costs associated with side effects are doubled.**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £14,769 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £12,636 |

**Sensitivity Analysis 12-1: Base-case, bar disutility and costs associated with side effects are halved.**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £13,999 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £11,860 |

**Sensitivity Analysis 13-1: Base-case, bar disutility and costs associated with side effects are set to zero.**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £13,745 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £11,611 |

**Sensitivity Analysis 14-1: Base-case, bar disutility from bisphosphonate side effects set to 10 times that of the base-case**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | £15,705 |
| 75 years and over | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £5,768 |

**Sensitivity Analysis 15-1: Base-case, bar costs associated with side effects increased to £8.78 per patient due to the assumption that proton pump inhibitors are prescribed instead of H2 receptor agonists**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £14,505 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £12,379 |

**Sensitivity Analysis 16-1: Base-case, bar intervention costs set to half of base-case (£132 per annum)**

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 65-69 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £17,193 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-0.5 SD | BMD and treat where T-Score <-0.0 SD | £13,036 |
| 75 years and over | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | BMD and treat where T-Score <0.0 SD | BMD and treat where T-Score <1.0 SD | £7,617 |

## 3.3 Detailed analysis for each scenario for women presenting with a self-identifying risk factor

The following matrices give the details for the age-bands where BMD scanning for sub-sets of women is considered cost-effective, at what T-Score to initiate treatment for each number of clinical risk factors (0-3) that a woman may have. The final column indicates the overall cost per QALY of a BMD and treatment strategy for the age-band, which by definition will be lower than £20,000. For those age bands not included the cost per QALY of an opportunistic screening, BMD and treatment strategy was greater than £20,000.
In these analyses a higher cost per QALY does not necessarily reflect that a strategy is less effective, but could imply that a strategy is more permissive in who is treated. Our methodology (see calculating cost per QALY on page 11) maximises the total net benefit by treating any patient with an individual cost per QALY below £20,000.
For example, if hypothetical scenario A was more favourable to the intervention than hypothetical scenario B, and thus allowed women in an additional T-Score band to be treated, where the cost per QALY was very close to the £20,000 threshold, it is likely that the overall cost per QALY of scenario A would be greater that that for B where women in this T-Score band were not treated and thus the average cost per QALY was lower.

**Scenario description: Base-case 2.**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £18,555 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £14,110 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £15,247 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £12,892 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £7,801 |

**Sensitivity Analysis 1-2: Base-case, bar persistence set to 25%**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-3.0 SD | £15,484 |
| 65 - 69 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £14,123 |
| 70-74 years | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | £11,732 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-0.5 SD | £9,039 |

**Sensitivity Analysis 2-2: Base-case, bar persistence set to 75%**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £17,927 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £14,247 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £13.055 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £12,298 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <0.0 SD | £7,442 |

**Sensitivity Analysis 3-2: Base-case, bar efficacy assumed to be different in the osteoporotic, osteopenic and normal women, and equal to that from the FIT trial.**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 50 - 54 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £14,307 |
| 55 - 59 years | Do not BMD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | £14,385 |
| 60-64 years | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | £13,915 |
| 65 - 69 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | £13,145 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | £8,159 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | £4,507 |

**Sensitivity Analysis 4-2: Base-case, bar efficacy of bisphosphonate set to 50% for clinical risk factor other than BMD and fracture status.**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 65 - 69 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-3.0 SD | £17,636 |
| 70-74 years | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £16,192 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | £10,507 |

**Sensitivity Analysis 5-2: Base-case, bar efficacy of bisphosphonate set to 0% for clinical risk factor other than BMD and fracture status. Questions on clinical risk factors are assumed not to be asked.**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 75 years and over | BMD and treat where T-Score <-3.5 SD | | | £18,569 |

**Sensitivity Analysis 6-2: Base-case, bar using the costs calculated by Stevenson et al to be used instead of the older costs, including potential home help costs.**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £15,592 |
| 60-64 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | £16,421 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £10,989 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £10,094 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <0.0 SD | £6,958 |

**Sensitivity Analysis 7-2: Base-case, bar using the costs calculated by Stevenson et al to be used instead of the older costs, excluding potential home help costs**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £16,259 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £12,913 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £12,347 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £11,296 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £6,212 |

**Sensitivity Analysis 8-2: Base-case, bar using HRG costs including potential home help costs**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £17,753 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £14,110 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £14,319 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £12,073 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £7,629 |

**Sensitivity Analysis 9-2: Base-case, bar using HRG costs excluding potential home help costs**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £19,088 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £13,712 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £15,686 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.0 SD | £13,386 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-0.5 SD | £8,892 |

**Sensitivity Analysis 10-2: Base-case, bar vertebral fracture disutility reduced to that of hip fracture**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £15,806 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | £16,265 |
| 70-74 years | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | £12,155 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £8,896 |

**Sensitivity Analysis 11-2: Base-case, bar disutility and costs associated with side effects are doubled.**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £19,146 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £14,655 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | £15,738 |
| 70-74 years | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £11,493 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-0.5 SD | £7,976 |

**Sensitivity Analysis 12-2: Base-case, bar disutility and costs associated with side effects are halved.**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £18,226 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £14,226 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £14,962 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £12,657 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £7,638 |

**Sensitivity Analysis 13-2: Base-case, bar disutility and costs associated with side effects are set to zero.**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £17,903 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £14,288 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £14,735 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £12,405 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £7,692 |

**Sensitivity Analysis 14-2: Base-case, bar disutility from bisphosphonate side effects set to 10 times that of the base-case**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £15,496 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | £16,485 |
| 70-74 years | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | £11,813 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £8,537 |

**Sensitivity Analysis 15-2: Base-case, bar costs associated with side effects increased to £8.78 per patient due to the assumption that proton pump inhibitors are prescribed instead of H2 receptor agonists**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £18,819 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £14,352 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £15,522 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £13,151 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-0.5 SD | £7,849 |

**Sensitivity Analysis 16-2: Base-case, bar intervention costs set to half of base-case (£132 per annum)**

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 50 - 54 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.0 SD | £16,765 |
| 55 - 59 years | Do not BMD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | £15,814 |
| 60-64 years | Do not BMD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £13,344 |
| 65 - 69 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £13,417 |
| 70-74 years | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | BMD and treat where T-Score <0.5 SD | £8,650 |
| 75 years and over | BMD and treat where T-Score <-0.5 SD | BMD and treat where T-Score <0.0 SD | BMD and treat where T-Score <1.0 SD | £5,047 |

## 4. Estimating the cost-effectiveness of opportunistic assessment and BMD scanning policies for other interventions for osteoporosis.

Alendronate and risedronate are not the only interventions available for the treatment of osteoporosis. We have also analysed the cost-effectiveness of strontium ranelate, etidronate, raloxifene, and teriparatide treatment of women with an identifying risk factor.

The assumed efficacies and costs of each intervention are provided in Table 3

Table 3. The assumed costs and efficacy of treatment for each intervention

| | | Efficacy (RR) on [11] | | | |
|---|---|---|---|---|---|
| | Cost per annum (£) [12] | Hip | Spine | Wrist | Proximal Humerus |
| Pooled alendronate and risedronate | 264 | 0.71 | 0.58 | 0.78 | 0.78 |
| Strontium ranelate | 334 | 0.85 | 0.60 | 0.84 | 0.84 |
| Etidronate | 90 | 1.00 | 0.40 | 1.00 | 1.00 |
| Raloxifene | 259 | 1.00 | 0.65 | 1.00 | 1.00 |
| Teriparatide | 3,546 | 0.50 | 0.35 | 0.65 | 0.65 |

Teriparatide is prescribed for 18 months, whilst all other interventions are assumed to be prescribed for 5 years.
Only RCT evidence for etidronate has been used. If observational data were included in the analyses [13] the cost per QALY would be significantly reduced.
On the request of the committee only fracture data for raloxifene has been considered. Any benefits the drug may have on breast cancer incidence and progression [14] have been excluded.

Due to the number of calculations required we have solely used the midpoint values for each intervention. For most interventions this will cause little bias in the mean cost per QALY as the relative risks are generally under unity. For teriparatide however, which has a large confidence interval for hip fracture efficacy (0.09 – 2.73) the use of the midpoint may produce favourable mean cost per QALYs, as the large number of fractures associated with the higher relative risks have not been incorporated.

[11] http://www.nice.org.uk/page.aspx?o=273846
[12] Taken from http://www.bnf.org/bnf/ BNF 51. Accessed 01/07/06.
[13] van Staa, T. P., Dennison, E. M., Leufkens, H. G., and Cooper, C. Epidemiology of fractures in England and Wales. *Bone* 2001; **29** 517-522.
[14] Cauley, J. A., Norton, L., Lippman, M. E., Eckert, S., Krueger, K. A., Purdie, D. W., Farrerons -J, Karasik, A., Mellstrom, D., Kong, Wah Ng, Stepan, J. J., Powles, T. J., Morrow, M., Costa, A., Silfen, S. L., Walls, E. L., Schmitt, H., Muchmore, D. B., and Jordan, V. C. Continued breast cancer risk reduction in postmenopausal women treated with raloxifene: 4-Year results from the MORE trial. *Breast Cancer Research & Treatment* 2001; **65** 124-134.

The cost per QALY gained for treating women identified by opportunistic assessment (section 4.1) and for treating women presenting with a self-identifying risk factor (section 4.2) was analysed for each drug. For these analyses it was assumed that the costs of opportunistic assessment (see page 10), and BMD scans where appropriate, would need to be borne from benefits accrued through use of the intervention. Additional analyses are presented in Section 5 that look at the cost-effectiveness thresholds of interventions that may be considered second-line treatments assuming that the costs of opportunistic assessment and BMD scanning has already been incurred.

Whilst some of the interventions may not be associated with upper GI problems each intervention has a side-effect profile (for example the increased risk of venous thrombosis). It was assumed that the costs and disutilities associated with these conditions were equal to those associated with pooled alendronate and risedronate. It is also assumed that persistence is 50% for all other drugs.

For completeness we have allowed teriparatide to be considered as an intervention for women who present without a self-identifying risk factor. This is because teriparatide has a marketing authorisation for women with previous fracture only, but a previous fracture could be established during the opportunistic assessment

## 4.1 Detailed analysis for each intervention following opportunistic assessment of clinical risk factors.

Summarised results are given in Table 4 followed by the individual results for each intervention. (Tables 5 to 9)

Table 4. Summarised strategies for each intervention for women *identified through opportunistic assessment* (base-case scenario).

| Intervention analysed | Identification strategies cost-effective from what age (years)? | Percentage of women age 50 or older that would be offered a BMD scan (%) [∇] | Percentage of women age 50 or older that would be treated (%) [∇ψ] |
|---|---|---|---|
| Pooled alendronate and risedronate | 70 | 25.7 | 2.5 |
| Strontium ranelate | 75 | 5.7 | 0.2 |
| Raloxifene | None | 0.0 | 0.0 |
| Etidronate | 70 | 25.7 | 9.1 |
| Teriparatide | 75 | 1.2 | 0.0 |

[∇] These are the BMD Scans and people treated assuming that all women with a prior fracture were opportunistically screened immediately. Once this had been achieved, the numbers will be significantly reduced, assuming that opportunistic assessment regarding clinical risk factors would be undertaken once every 5 years, and that people on treatment would not be re-assessed.

[ψ] These numbers have taken persistence into account. Thus, where persistence is 50%, double this number would be offered treatment.

Table 5. The base-case results for pooled alendronate and risedronate in women identified by opportunistic assessment. (same as matrix 'base-case 1' on page 17)

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.5 SD | £14,257 |
| 75 years and over | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £12,113 |

Table 6. The base-case results for strontium ranelate in women identified by opportunistic assessment.

| Age (years) | 0 Clinical Risk Factor | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 75 years and over | Do not BMD | BMD and treat where T-Score <-3.5 SD | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | £15,848 |

Table 7. The base-case results for raloxifene in women identified by opportunistic assessment.

Opportunistic assessment strategies have cost per QALYs of >£20,000 at all ages.

Table 8. The base-case results for etidronate in women identified by opportunistic assessment.

| Age (years) | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 70-74 years | Do not BMD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | BMD and treat where T-Score <1.0 SD | £17,064 |
| 75 years and over | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-1.0 SD | BMD and treat where T-Score <0.0 SD | BMD and treat where T-Score <1.0 SD | £16,490 |

Table 9. The base-case results for teriparatide in women identified by opportunistic assessment.

| Age (years) | 0 Clinical Risk Factor | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | Cost Per QALY of strategy |
|---|---|---|---|---|---|
| 75 years and over | Do not BMD | Do not BMD | BMD and treat where T-Score <-4.0 SD | BMD and treat where T-Score <-3.0 SD | £16,830 |

Illustrative cost per QALY values for each intervention compared with no treatment are given in Table 10 for women of different ages, at a T-Score in the range –2.5 to –3.0 SD, assuming that they have no clinical risk factors. These values include neither the costs of assessment nor the costs of BMD scanning.

Table 10. Cost per QALY values for each intervention compared with no treatment. For women with a T-Score in the range –2.5 to –3.0 SD and no clinical risk factors.

| | 50 | 60 | 70 | 75 |
|---|---|---|---|---|
| Pooled alendronate and risedronate | £108,643 | £75,014 | £33,787 | £25,539 |
| Strontium ranelate | £218,040 | £140,125 | £57,939 | £47,144 |
| Raloxifene | £788,772 | £312,558 | £83,367 | £70,977 |
| Etidronate | £124,373 | £59,866 | £17,243 | £13,744 |
| Teriparatide | £522,441 | £369,429 | £179,154 | £148,713 |

Table 11 gives the incremental cost-effectiveness of moving from each intervention to pooled alendronate and risedronate. Pooled alendronate and risedronate is considered more cost-effective than both strontium ranelate and raloxifene. However because of the lower price of etidronate a move from etidronate to pooled alendronate and risedronate would not be considered cost-effective as the cost per QALY ratio is greater than £60,000 in the examples provided.

Table 11. Cost per QALY values for pooled alendronate and risedronate compared with each intervention. For women with a T-Score in the range –2.5 to –3.0 SD and no clinical risk factors.

| | 50 | 60 | 70 | 75 |
|---|---|---|---|---|
| Strontium ranelate | Pooled alendronate and risedronate dominates strontium ranelate | Pooled alendronate and risedronate dominates strontium ranelate | Pooled alendronate and risedronate dominates strontium ranelate | Pooled alendronate and risedronate dominates strontium ranelate |
| Raloxifene | Pooled alendronate and risedronate dominates raloxifene | Pooled alendronate and risedronate dominates raloxifene | Pooled alendronate and risedronate dominates raloxifene | Pooled alendronate and risedronate dominates raloxifene |
| Etidronate | £100,142 | £90,474 | £102,328 | £64,517 |
| Teriparatide * | £4.7 m | £3.9 m | £2.5 m | £2.0 m |

* Teriparatide provides more QALYs than pooled alendronate and risedronate, but costs more. In this circumstance cost per QALY ratios greater than £20,000 are desirable.

There is thus a case, given our current efficacy and pricing assumptions that etidronate could be considered the most cost-effective treatment. The strategy for opportunistically assessing women and subsequently providing BMD scans for women with a self-identifying fracture is however unaffected by the choice of bisphosphonate, i.e. it is identical for the pooled alendronate and risedronate and for etidronate and is thus unaffected by whichever intervention was chosen as first line treatment. From our data, etidronate could be cost-effectively prescribed to women at less severe T-Score thresholds than pooled alendronate and risedronate.

## 4.2 Detailed analysis for each intervention for women presenting with a self-identifying risk factor.

Summarised results are given in Table 12 followed by the individual results for each intervention. (Tables 13 to 17)

Table 12. Summarised strategies for each intervention for women presenting with a self- identifying risk factor (base-case scenario)

| Intervention analysed | BMD scanning strategies cost-effective from what age (years)? | Percentage of women age 50 or older that would be offered a BMD scan (%) $^{\nabla}$ | Percentage of women age 50 or older that would be successfully treated (%) $^{\nabla\Psi}$ |
|---|---|---|---|
| Pooled alendronate and risedronate | 55 | 58.2 | 12.6 |
| Strontium ranelate | 65 | 44.1 | 3.5 |
| Raloxifene | None | 0.0 | 0.0 |
| Etidronate | 55 | 58.2 | 27.5 |
| Teriparatide | 70 | 2.5 | 0.1 |

$^{\nabla}$ These are the BMD Scans and people treated assuming that all women with a prior fracture were opportunistically screened immediately. Once this had been achieved, the numbers will be significantly reduced, assuming that opportunistic assessment regarding clinical risk factors would be undertaken once every 5 years, and that people on treatment would not be re-assessed.

$^{\Psi}$ These numbers have taken persistence into account. Thus, where persistence is 50%, double this number would be offered treatment.

Table 13. The base-case results for pooled alendronate and risedronate in women with a one self-identifying risk factor (same as matrix 'base-case 2' on page 24)

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £18,555 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-2.5 SD | £14,110 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £15,247 |
| 70-74 years | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-1.0 SD | £12,892 |
| 75 years and over | BMD and treat where T-Score <-2.5 SD | BMD and treat where T-Score <-1.5 SD | BMD and treat where T-Score <-0.5 SD | £7,801 |

Table 14. The base-case results for strontium ranelate in women with one self-identifying risk factor.

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 65 - 69 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-3.0 SD | £19,623 |
| 70-74 years | Do not BMD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-2.0 SD | £14,816 |
| 75 years and over | BMD and treat where T-Score <-3.5 SD | BMD and treat where T-Score <-3.0 SD | BMD and treat where T-Score <-1.5 SD | £12,660 |

Table 15. The base-case results for raloxifene in women with one self- identifying risk factor.

Opportunistic assessment strategies have cost per QALYs of >£20,000 at all ages.

Table 16. The base-case results for etidronate in women with one self-identifying risk factor.

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 55 - 59 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-1.5 SD | £16,858 |
| 60-64 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-1.5 SD | £16,960 |
| 65 - 69 years | Do not BMD | BMD and treat where T-Score <-2.0 SD | BMD and treat where T-Score <-0.5 SD | £16,281 |
| 70-74 years | BMD and treat where T-Score <-0.0 SD | BMD and treat where T-Score <1.0 SD | BMD and treat where T-Score <1.0 SD | £12,629 |
| 75 years and over | BMD and treat where T-Score <0.5 SD | BMD and treat where T-Score <1.0 SD | BMD and treat where T-Score <1.0 SD | £9,869 |

Table 17. The base-case results for teriparatide in women with one self-identifying risk factor.

| Age (years) | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors | CPQ of strategy |
|---|---|---|---|---|
| 70-74 years | Do not BMD | Do not BMD | BMD and treat where T-Score <-3.5 SD | £14,051 |
| 75 years and over | Do not BMD | Do not BMD | BMD and treat where T-Score <-3.5 SD | £11,280 |

Illustrative cost per QALY values for each intervention compared with no treatment are given in Table 18 for women of different ages, at a T-Score in the range –2.5 to –3.0 SD, assuming that they have one self-identifying risk factor. These values include neither the costs of assessment nor the costs of BMD scanning.

Table 18. Cost per QALY values for each intervention compared with no treatment. For women with a T-Score in the range –2. 5 to –3.0 SD and one self-identifying risk factor.

| | 50 | 60 | 70 | 75 |
|---|---|---|---|---|
| Pooled alendronate and risedronate | £48,521 | £38,821 | £19,179 | £14,926 |
| Strontium ranelate | £99,056 | £73,776 | £33,971 | £28,791 |
| Raloxifene | £289,465 | £153,113 | £48,583 | £42,883 |
| Etidronate | £55,787 | £31,173 | £9,834 | £8,039 |
| Teriparatide | £246,896 | £201,238 | £109,130 | £95,397 |

Table 19 gives the incremental cost-effectiveness of moving from each intervention to pooled alendronate and risedronate. Pooled alendronate and risedronate is considered more cost-effective than both strontium ranelate and raloxifene. However because of the lower price of etidronate a move from etidronate to pooled alendronate and risedronate would not be considered cost-effective as the cost per QALY ratio is greater than £30,000 in the examples provided.

Table 19. Cost per QALY values for pooled alendronate and risedronate compared with each intervention. For women with a T-Score in the range –2.5 to –3.0 SD and one self-identifying risk factor.

| | 50 | 60 | 70 | 75 |
|---|---|---|---|---|
| Strontium ranelate | Pooled alendronate and risedronate dominates strontium ranelate | Pooled alendronate and risedronate dominates strontium ranelate | Pooled alendronate and risedronate dominates strontium ranelate | Pooled alendronate and risedronate dominates strontium ranelate |
| Raloxifene | Pooled alendronate and risedronate dominates raloxifene | Pooled alendronate and risedronate dominates raloxifene | Pooled alendronate and risedronate dominates raloxifene | Pooled alendronate and risedronate dominates raloxifene |
| Etidronate | £44,268 | £47,237 | £65,087 | £43,766 |
| Teriparatide * | £2.3 m | £2.2 m | £1.6 m | £1.4 m |

* Teriparatide provides more QALYs than pooled alendronate and risedronate, but costs more. In this circumstance cost per QALY ratios greater than £20,000 are desirable.

As in the case of women identified by opportunistic assessment, the current efficacy and pricing assumptions mean that etidronate could be considered the most cost-

effectiveness treatment. The strategy for providing BMD scans for women with a self-identifying fracture is however unaffected by the choice of bisphosphonate, i.e. it is identical for the pooled alendronate and risedronate and for etidronate and is thus unaffected by whichever intervention was chosen as first line treatment. From our data, etidronate could be cost-effectively prescribed to women at less severe T-Score thresholds than pooled alendronate and risedronate.

## 5. Estimating the cost-effectiveness of potential second line interventions

Based on the current guidance for the secondary prevention of osteroporotic fracture[15] and previous appraisal consultation documents[16,17], it is conceivable that an analysis for second-line interventions is required. For women who have been identified, the number of risk factors summated, a BMD scan performed and begun treatment on alendronate or risedronate but cannot tolerate this intervention, the T-Score threshold at which other interventions become cost-effective has therefore been calculated. In this circumstance no additional assessment or BMD scanning costs are incurred as these costs have already been accounted for, i.e. that the risk factors and BMD of women considered for pooled alendronate and risedronate treatment are already known. In this instance only the cost-effectiveness of treatment itself is relevant.

As an example, in isolation strontium ranelate is cost effective for women aged 70 years with 3 clinical risk factors (none of which were self-identifying). However if strontium was considered as the first line therapy these patients would not be treated as the costs of opportunistically assessing and then providing BMD scans to women with 3 clinical risk factors were prohibitive. Where pooled alendronate and risedronate were assumed first line therapy, women can be cost-effectively assessed and those with 3 clinical risk factors provided with BMD scans. If women with T-scores <-2.5 SD could not tolerate bisphosphonates then strontium ranelate could be cost-effectively initiated.

The T-Score thresholds may differ between women previous identified by opportunistic screening and those presenting with a self-identifying risk factor as the coefficient of increased risk for future fractures is different between clinical risk factors. As such the T-Score thresholds are presented separately for women who were identified by opportunistic assessment and for those with self-identifying risk factors.

For comparative purposes the T-Score threshold at which pooled alendronate and risedronate is considered a cost-effective treatment is provided in italics in the tables.

[15] http://www.nice.org.uk/page.aspx?o=TA087
[16] http://www.nice.org.uk/page.aspx?o=273457
[17] http://www.nice.org.uk/page.aspx?o=273846

## 5.1 T-Score threshold analysis for each intervention for women who had previously been identified by opportunistic assessment.

Using pooled alendronate and risedronate as a first-line treatment, at a cost per QALY of £20,000 it was considered cost-effective to opportunistically assess all women aged 70 years and over and to BMD scan all these women bar those aged 70-74 years and without a clinical risk factor. Using this strategy as a base-case the T-Score thresholds at which women that had previously been identified by opportunistic assessment could be cost effectively treated with an alternative intervention is given in Tables 20 and 21.

The most negative T-Score that was analysed was women in the group –5.0 to –5.5SD since very few women have T-Scores more severe than this. Where the cost per QALY of an intervention was greater than £20,000 for women with T-Scores of -4.75 to -5.25SD, the phrase "Cost per QALY >£20,000 for all T-Scores" has been used in the tables.

Table 20. Treatment thresholds for which each intervention can be considered cost-effective in women aged 70-74 years of age who had previously been identified by opportunistic assessment.

| | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors |
|---|---|---|---|
| *Pooled alendronate and risedronate* | *Treat where T-Score <-3.0 SD* | *Treat where T-Score <-2.0 SD* | *Treat where T-Score <-1.5 SD* |
| Strontium ranelate | Treat where T-Score <-4.0 SD | Treat where T-Score <-3.0 SD | Treat where T-Score <-2.5 SD |
| Raloxifene | Cost per QALY >£20,000 for all T-Scores | Treat where T-Score <-5.0 SD | Treat where T-Score <-4.5 SD |
| Etidronate | Treat where T-Score <-1.5 SD | Treat where T-Score <-0.5 SD | Treat where T-Score <1.0 SD |
| Teriparatide | Treat where T-Score <-5.0 SD | Treat where T-Score <-4.5 SD | Treat where T-Score <-3.5 SD |

Table 21. Treatment thresholds for which each intervention can be considered cost-effective in women aged 75-79 years of age who had previously been identified by opportunistic assessment.

| | 0 Clinical Risk Factors | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors |
|---|---|---|---|---|
| *Pooled alendronate and risedronate* | *Treat where T-Score <-3.0 SD* | *Treat where T-Score <-2.5 SD* | *Treat where T-Score <-1.5 SD* | *Treat where T-Score <-0.5 SD* |
| Strontium ranelate | Treat where T-Score <-4.0 SD | Treat where T-Score <-3.5 SD | Treat where T-Score <-2.5 SD | Treat where T-Score <-2.0 SD |
| Raloxifene | Cost per QALY >£20,000 for all T-Scores | Cost per QALY >£20,000 for all T-Scores | Treat where T-Score <-5.0 SD | Treat where T-Score <-4.0 SD |
| Etidronate | Treat where T-Score <-1.5 SD | Treat where T-Score <-1.0 SD | Treat where T-Score <0.0 SD | Treat where T-Score <1.0 SD |
| Teriparatide | Cost per QALY >£20,000 for all T-Scores | Treat where T-Score <-5.0 SD | Treat where T-Score <-4.0 SD | Treat where T-Score <-3.0 SD |

## 5.2 T-Score threshold analysis for each intervention for women who had previously presented with a self-identifying risk factor.

Assuming pooled alendronate and risedronate as a first-line treatment, at a cost per QALY threshold of £20,000 it was considered cost-effective to selectively BMD scan all women aged 55 years and over. As age increased the number of clinical risk factors required to receive a BMD scan decreased. Using this strategy as a base-case the T-Score thresholds at which women that had previously been identified by opportunistic assessment could be cost effectively treated with an alternative intervention is given in Tables 22 and 26.

Table 22. Treatment thresholds for which each intervention can be considered cost-effective in women aged 55-59 years of age who had previously presented with a self-identifying risk factor.

| | 3 Clinical Risk Factors |
|---|---|
| *Pooled alendronate and risedronate* | *Treat where T-Score <-2.5 SD* |
| Strontium ranelate | Treat where T-Score <-3.5 SD |
| Raloxifene | Cost per QALY >£20,000 for all T-Scores |
| Etidronate | Treat where T-Score <-1.5 SD |
| Teriparatide | Treat where T-Score <-4.0 SD |

Table 23. Treatment thresholds for which each intervention can be considered cost-effective in women aged 60-64 years of age who had previously presented with a self-identifying risk factor.

| | 3 Clinical Risk Factors |
|---|---|
| *Pooled alendronate and risedronate* | *Treat where T-Score <-2.5 SD* |
| Strontium ranelate | Treat where T-Score <-3.5 SD |
| Raloxifene | Cost per QALY >£20,000 for all T-Scores |
| Etidronate | Treat where T-Score <-1.5 SD |
| Teriparatide | Treat where T-Score <-4.0 SD |

Table 24. Treatment thresholds for which each intervention can be considered cost-effective in women aged 65-69 years of age who had previously presented with a self-identifying risk factor.

| | 2 Clinical Risk Factors | 3 Clinical Risk Factors |
|---|---|---|
| *Pooled alendronate and risedronate* | *Treat where T-Score <-3.0 SD* | *Treat where T-Score <-2.0 SD* |
| Strontium ranelate | Treat where T-Score <-4.0 SD | Treat where T-Score <-3.0 SD |
| Raloxifene | Cost per QALY >£20,000 for all T-Scores | Cost per QALY >£20,000 for all T-Scores |
| Etidronate | Treat where T-Score <-2.0 SD | Treat where T-Score <-0.5 SD |
| Teriparatide | Treat where T-Score <-5.0 SD | Treat where T-Score <-4.5 SD |

Table 25. Treatment thresholds for which each intervention can be considered cost-effective in women aged 70-74 years of age who had previously presented with a self-identifying risk factor.

| | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors |
|---|---|---|---|
| *Pooled alendronate and risedronate* | *Treat where T-Score <-2.5 SD* | *Treat where T-Score <-2.0 SD* | *Treat where T-Score <-1.0 SD* |
| Strontium ranelate | Treat where T-Score <-3.5 SD | Treat where T-Score <-3.0 SD | Treat where T-Score <-2.0 SD |
| Raloxifene | Treat where T-Score <-5.0 SD | Treat where T-Score <-4.5 SD | Treat where T-Score <-4.0 SD |
| Etidronate | Treat where T-Score <0.0 SD | Treat where T-Score <1.0 SD | Treat where T-Score <1.0 SD |
| Teriparatide | Treat where T-Score <-5.0 SD | Treat where T-Score <-4.5 SD | Treat where T-Score <-3.5 SD |

Table 26. Treatment thresholds for which each intervention can be considered cost-effective in women aged 75 years of age and older who had previously presented with a self-identifying risk factor.

| | 1 Clinical Risk Factor | 2 Clinical Risk Factors | 3 Clinical Risk Factors |
|---|---|---|---|
| *Pooled alendronate and risedronate* | *Treat where T-Score <-2.5 SD* | *Treat where T-Score <-1.5 SD* | *Treat where T-Score <-0.5 SD* |
| Strontium ranelate | Treat where T-Score <-3.5 SD | Treat where T-Score <-3.0 SD | Treat where T-Score <-1.5 SD |
| Raloxifene | Treat where T-Score <-4.5 SD | Treat where T-Score <-4.5 SD | Treat where T-Score <-3.5 SD |
| Etidronate | Treat where T-Score <0.5 SD | Treat where T-Score <1.0 SD | Treat where T-Score <1.0 SD |
| Teriparatide | Treat where T-Score <-5.0 SD | Treat where T-Score <-4.5 SD | Treat where T-Score <-3.5 SD |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# Appendix 1.

# Meta-analysis of clinical effectiveness data for alendronate & risedronate

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June 2006

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## Introduction

At the request of the Appraisal Committee, clinical effectiveness data for alendronate and risedronate were meta-analysed to give a single estimate of efficacy at each fracture site for these two technologies.

## Methods

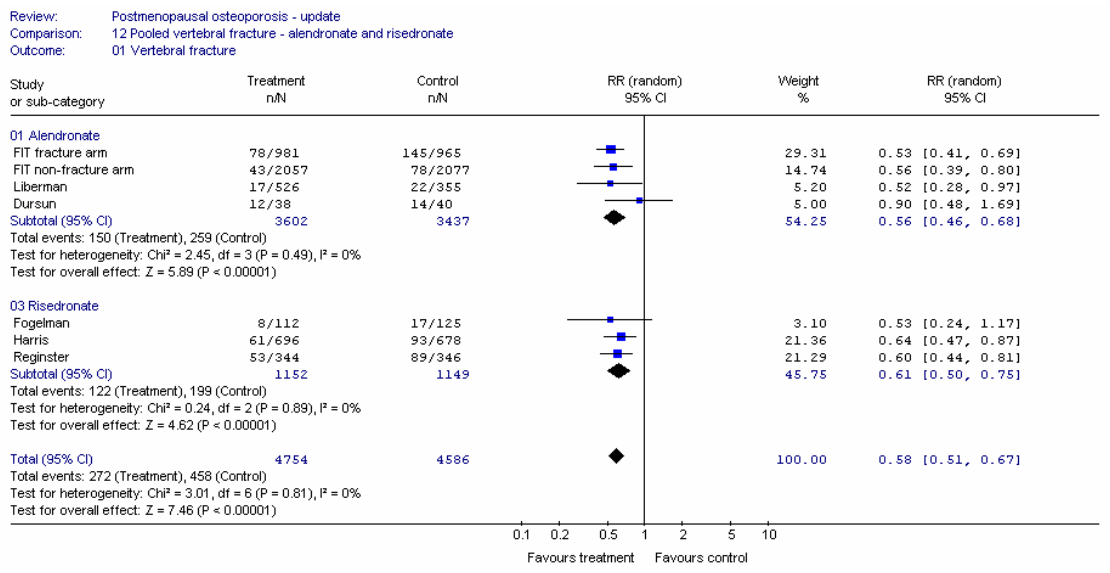
The clinical effectiveness data were obtained by systematic review. The methods and results of systematic reviews and meta-analyses conducted separately for alendronate and risedronate can be found in the first Assessment Report relating to this appraisal, now published as a HTA monograph[18]. The systematic review was updated for a DSU report in 2005[19]. This report contains details of new studies and updated meta-analyses.

Meta-analysis was carried out using Review Manager using the random-effects model, as this both allows generalisation beyond the sample of patients represented by the studies included in the meta-analysis and provides wider, more conservative confidence intervals than the fixed-effects model.

## Results

The results of the meta-analyses are presented below.

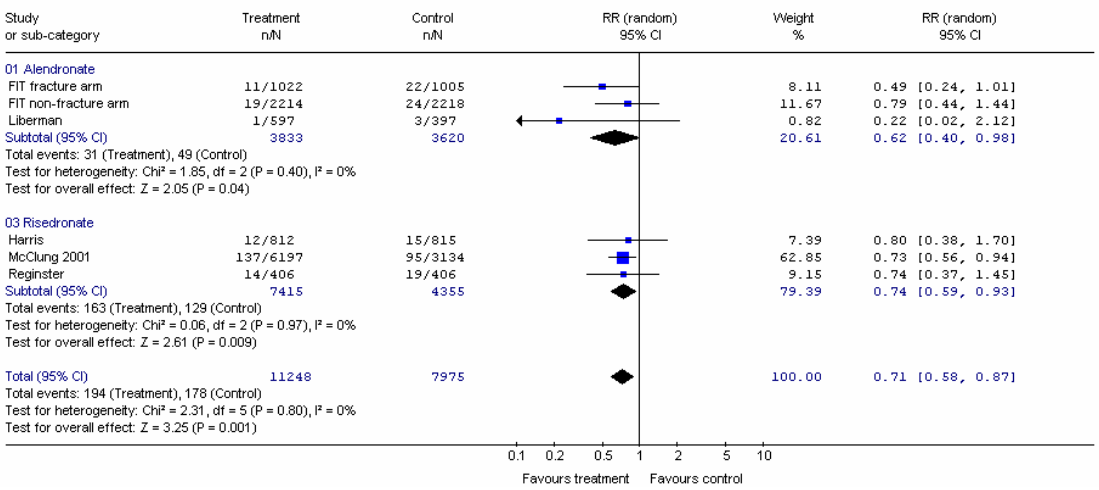
## Vertebral fracture




[18] http://www.ncchta.org/fullmono/mon922.pdf
[19] http://www.nice.org.uk/page.aspx?o=273738

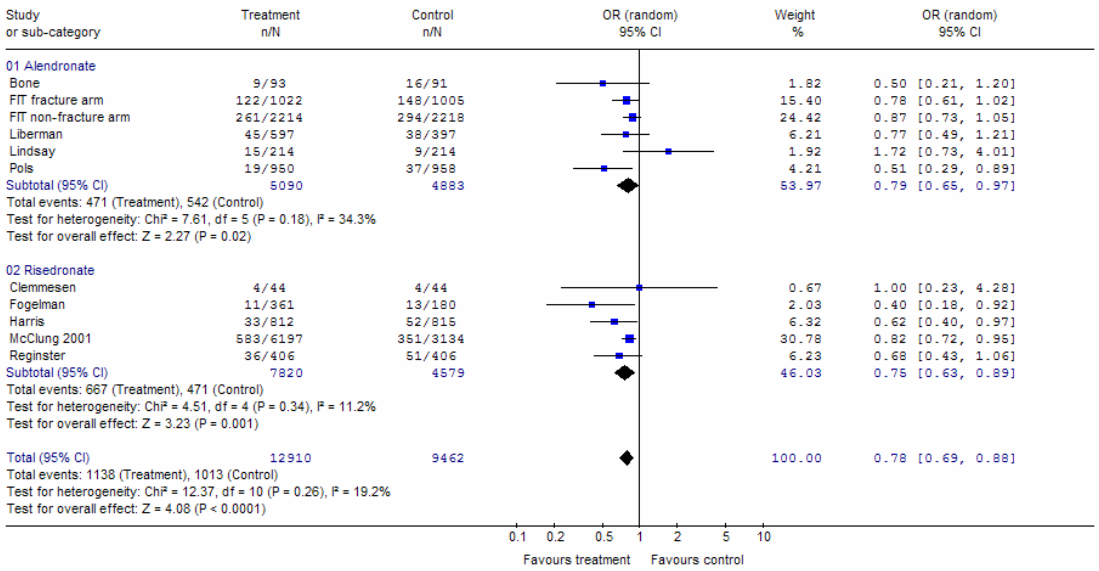
# Hip fracture

Review: Postmenopausal osteoporosis - update
Comparison: 13 Pooled hip fracture - alendronate and risedronate
Outcome: 01 Hip fracture

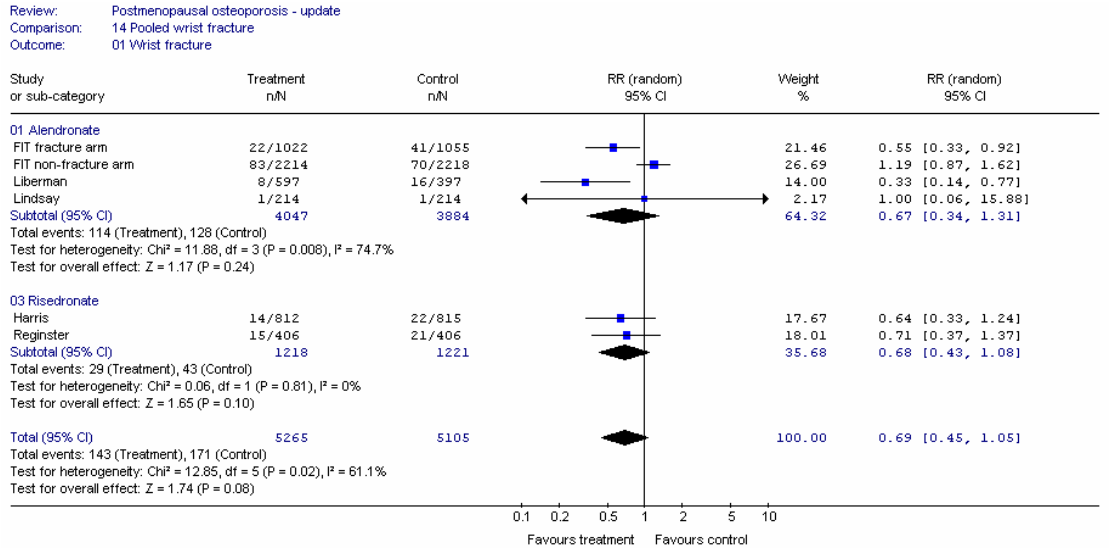



# Proximal humerus (Assumed equal to all non-vertebral fractures)

Review: Postmenopausal osteoporosis: alendronate + risedronate
Comparison: 01 Pooled prox humerus etc fracture
Outcome: 01 Prox humerus etc fracture



## Wrist fracture




## Note on fracture sites not at the vertebral or hip

Where data was available for all non-hip fractures this was used in preference to individual proximal humerus or wrist data for two reasons. Firstly the expansion of wrist and proximal humerus to include fractures at the tibia, fibula, clavicle, scapula, rib, proximal humerus shaft and sternum would mean that all non-vertebral fractures was a better measure, and secondly the larger number of fractures expected would reduce the width of the confidence interval for the relative risk of intervention. In our analyses all non-vertebral fractures is shown in the forest plot above with a mean of 0.78 (confidence interval 0.69 – 0.88)


The University Of Sheffield.

# Appendix 2.

# Estimating the costs of fracture based on updated evidence.

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June 2006

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Introduction.

The costs used in previous assessments were originally sourced from Dolan and Torgerson [1] These have become dated and more recent literature show that the costs of hip and vertebral fracture may be significantly higher than previously estimated. [2] [3]

Health Resource Group (HRG) data is also available, which indicates that the costs for hip fracture have declined, although costs for additional fractures may be higher dependent upon which HRG group is chosen to represent each facture type.

This appendix details two approaches in estimating the costs of fracture. The first, a simplification of which is in press, [4] uses length of stay data and cost per bed day to estimate fracture costs. The second approach estimates fractures using an HRG approach. The costs from the former approach are lower than those in the literature but greater than those estimated through HRG analyses.

Summary tables of the costs used in the base-case and the two sensitivity analyses are provided, followed by the details of each methodology.

Base-case costs. Taken from the strontium ranelate NICE assessment report. [5]

**Table A1 The costs of each event, by age and by initial and subsequent years.**

| | Ages 50 – 54 costs (£) | | Ages 60 - 64 costs (£) | | Ages 70 – 74 costs (£) | | Ages 80 - 84 costs (£) | |
|---|---|---|---|---|---|---|---|---|
| State | 1st year costs | Subsequent annual costs | 1st year costs | Subsequent annual costs | 1st year costs | Subsequent annual costs | 1st year costs | Subsequent annual costs |
| Hip Fracture * | 5,157 | - | 5,157 | - | 6,487 | - | 8,538 | - |
| Vertebral Fracture | 477 | 222 | 477 | 222 | 539 | 222 | 581 | 222 |
| Wrist Fracture ** | 359 | - | 359 | - | 359 | - | 585 | - |
| Proximal Humerus Fracture *** | 1,024 | - | 1,024 | - | 1,024 | - | 1,674 | - |

* Assumed applicable for pelvis and other femoral fracture

** Assumed applicable for rib, sternum, clavicle and scapula

*** Assumed applicable for tibia, fibula and humeral shaft fractures

Costs estimated by Stevenson et al.

**Table A2 The costs of each event, by age and by initial and subsequent years.**

| | Ages 50 – 54 costs (£) | | Ages 60 - 64 costs (£) | | Ages 70 – 74 costs (£) | | Ages 80 - 84 costs (£) | |
|---|---|---|---|---|---|---|---|---|
| State | 1st year costs | Subsequent annual costs | 1st year costs | Subsequent annual costs | 1st year costs | Subsequent annual costs | 1st year costs | Subsequent annual costs |
| Hip Fracture * | 7,889 | - | 7,889 | - | 9,196 | - | 14,529 | - |
| Vertebral Fracture ** | 1,967 | 348 | 1,967 | 306 | 1,967 | 484 | 1,967 | 1,014 |
| Wrist Fracture *** | 901 | - | 901 | - | 901 | - | 901 | - |
| Proximal Humerus Fracture **** | 2,212 | - | 1,776 | - | 1,660 | - | 1,564 | - |

* Assumed applicable for pelvis and other femoral fracture

** The subsequent annual costs have been increased to take into account a small proportion of vertebral fractures requiring admission to a nursing home.

** Assumed applicable for rib, sternum, clavicle and scapula

*** Assumed applicable for tibia, fibula and humeral shaft fractures

The relative incidences of each fracture type will affect the overall cost at an age group. For example the average cost per 'proximal humerus' fracture decreases as age increases as a smaller proportion of the fractures are the more costly tibia and fibula fractures.

These costs exclude home help requirements. Were these included we have assumed additional costs of £1,143 for hip, £1,699 for vertebral fractures and £85 for wrist fractures. For 'proximal humerus' fractures tibia and fibula fractures were assumed to incur home help costs of £1,143 whilst the remaining fractures incurred costs of £85. (see text for more details)

Costs estimated by Health Resource Group values.

**Table A2 The costs of each event, by age and by initial and subsequent years.**

| | Ages 50 – 54 costs (£) | | Ages 60 - 64 costs (£) | | Ages 70 – 74 costs (£) | | Ages 80 - 84 costs (£) | |
|---|---|---|---|---|---|---|---|---|
| State | 1st year costs | Subsequent annual costs | 1st year costs | Subsequent annual costs | 1st year costs | Subsequent annual costs | 1st year costs | Subsequent annual costs |
| Hip Fracture * | 4,553 | - | 4,553 | - | 5,607 | - | 5,607 | - |
| Vertebral Fracture ** | 639 | 222 | 639 | 222 | 1,061 | 222 | 1,061 | 222 |
| Wrist Fracture *** | 629 | - | 808 | - | 1,118 | - | 877 | - |
| Proximal Humerus Fracture **** | 1,730 | - | 1,198 | - | 1,508 | - | 1,419 | - |

* Assumed applicable for pelvis and other femoral fracture

** The subsequent annual costs have been increased to take into account a small proportion of vertebral fractures requiring admission to a nursing home.

** Assumed applicable for rib, sternum, clavicle and scapula

*** Assumed applicable for tibia, fibula and humeral shaft fractures

The relative incidences of each fracture type will affect the overall cost at an age group. For example the average cost per 'proximal humerus' fracture decreases as age increases as a smaller proportion of the fractures are the more costly tibia and fibula fractures.

These costs exclude home help requirements. Were these included we have assumed additional costs of £1,143 for hip, £1,699 for vertebral fractures and £85 for wrist fractures. For 'proximal humerus' fractures tibia and fibula fractures were assumed to incur home help costs of £1,143 whilst the remaining fractures incurred costs of £85. (see text for more details)

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**Appendix 2a**

**The methodology for estimating the costs of fracture using length of stay and cost per bed day data.**

General Comments.

An adaptation of this work is in press (as of July 2006).

Cost per day in an orthopaedic bed.

Standard sources do not contain the cost of an orthopaedic bed-day. What we do have are the costs of bed days for elderly patients charged at £159 per day. [6] From Swedish data the costs of an orthopaedic bed is €700 per day, whilst geriatric beds cost €374 per day. [7] If the same ratio is applied to the English data, it is estimated that the cost of an orthopaedic bed would be £298 per day. We have currently used the cost of an orthopaedic bed-day for all fracture types. However should a proportion of these patients be treated in geriatric wards our costs will be an overestimate

Length of stay data.

We have tried to cost each fracture using Hospital Episode Statistics (HES) data for 2002 – 2004. Where there HES groupings may make the use of this methodology non-robust, we have used length of stay data from Sweden [8] and commented on the reasons for this in the text. Comparisons of the length of stay for hip fracture in the UK from HES data and in Sweden are 26 days and 13 days respectively, suggest that where Swedish data are used to estimate length of stay the costs produced may be conservative.

Out-patient care costs.

We have assumed that following a fracture the same out-patient resources will be used regardless of whether a patient was hospitalised or not. These comprise costs for outpatient surgery, physician visits, nurse visits, physiotherapy, x-rays and phone help. Using Swedish data, we have calculated the ratio of the bed day cost for an average hospitalisation, to the out-patient care costs and assumed that this is applicable to the UK. These were an additional 11%, 9% and 31% for hip, vertebral and wrist respectively.

Home help costs

The costs for home help following a fracture will be heavily dependent of the health resources within a region and on whether the patient chooses to pay for their own help. Previously home help costs have not been included within the cost values. Questioning a small number of clinicians on the NICE Appraisal Committee and on the Guideline Development Group, it appears that 2 hours a day for 8 weeks following a hip fracture would not be unreasonable. Similar resources are required for vertebral, and for wrist and proximal humerus fractures, where the dominant arm has been fractured. Assuming costs of £14 per hour for home-care this would imply

additional home help costs of £1,568 for hip and vertebral fractures and £784 for wrist and proximal humerus fractures.
An alternative source for the amount of home-help required is Borgstrom et al, which is Swedish data. This estimates home help costs to be £1,143, £1,699 and £85 for hip, vertebral and wrist fractures respectively. We have used the Borgstrom data as this has been empirically collected, and is likely to be conservative compared with our estimated UK values.

Hospitalisation rates following a fracture.

Where possible we have used UK data for estimating the percentage of fractures that require hospitalisation. [9] Where this data is not available the percentage has been estimated assuming that data from Sweden is applicable for the UK. We have calculated the rates for Sweden from Census data, [10] hospitalisation data and incidence data. Where both Swdish and UK data are known, the Swedish value is typically lower, thus using Swedish data as a proxy is likely to be conservative.

**Hip Fracture.**

This also includes pelvis and other femoral fractures.

The average length of stay from HES data for 2002 - 2004 for fracture of femur is 26.0 days. The mean length of stay for pelvis is combined with lumbar spine (19.2 days) but the length of stay for pelvis fracture cannot be disentangled and it is unclear whether other femoral fractures are included in the femur fracture code.
Swedish data show that the length of stays for pelvis and other femoral fractures were 87% and 135% that of hip fracture. However the ratios of the incidences of pelvis to other femoral is 25:17 meaning that the combined length of stay are only slightly greater than that for hip fracture alone.
Given the possibility of the inclusion of other femoral fractures within the HES data we have assumed that the mean length of stay for all hip, pelvis and other femoral fractures is 26 days.

We would thus expect direct medical inpatient stay costs to be 26 * £298 = £7,748. Additional costs due to surgery, radiological tests and laboratory investigations amount to an estimated £1,947 per patient. [11] This would equal a total direct medical cost of £9,695 per patient.

Out-patient care for all patients with a hip fracture has been assumed to cost £1,066 (£9,695 * 11%).

Thus total inpatient and outpatient costs are estimated to be £10,761

If these were weighted by age in accordance with Swedish data we would expect cost values to be.

| Age Range (years) | Updated costs for hip fracture (£) | Updated costs for hip fracture including home help (£) |
|---|---|---|
| 50 – 64 | 7,889 | 9,032 |
| 65 – 74 | 9,196 | 10,339 |
| 75 – 84 | 9,776 | 10,919 |
| 85 + | 14,529 | 15,672 |

Note that these figures are lower than those reported in Lawrence that an average hip fracture costs at a Nottingham hospital, which were approximately £12,000 for direct medical costs only.

**Additional Costs associated with admission to a nursing home following a hip fracture.**

The cost of nursing home is assumed to be approximately £24,000 per annum, although this varies with age. The percentage of patients admitted to a nursing home, using Swedish data are provided, along with the previously used estimates. It is believed that the English data are likely to be under-estimates as women who initially return to the community, but shortly after enter a nursing home are not counted.

| Age Range (years) | Percentage of hip fractures that cause the patient to enter nursing home. (Swedish Data) | Percentage of hip fractures that cause the patient to enter nursing home. (English Data) |
|---|---|---|
| 50 – 59 | 6.7 | 0 |
| 60 – 69 | 6.5 | 4 |
| 70 – 79 | 10.2 | 4 |
| 80 – 89 | 14.7 | 12 |

In the earlier ages, the Swedish data equate to 1/13 women with a hip fracture being forced into a nursing home.

**Vertebral Fracture**

The average length of stay from Hospital Episode Statistics (HES) data for 2003/4 for fractures for lumbar spine and pelvis combined is 19.4 days. For fractures of ribs, sternum and thoracic spine this is 11.1 days.

The length of stay in Sweden is pelvis (11.9 days) spine (9.8 days) ribs and sternum (5.9 days). The numbers of fractures were pelvis (3,246) spine (4,737) ribs and sternum (1,911). Given these relative incidences and length of stays we have estimated that the mean length of stay for all 'vertebral' fractures in the UK is 15 days.

Given these assumptions we would expect direct medical inpatient stay costs to be 15 * £298 = £4,470 per hospitalised vertebral fracture.

Assuming that out-patient care is equal to 9% of direct medical costs, this would equate to an estimated total cost of vertebral fracture of £402 per patient with a vertebral fracture.

Thus a hospitalised fracture is estimated to cost £4,872 and a non-hospitalised fracture £402.

If it were assumed that 35% of clinical vertebral fractures are hospitalised (Kanis & Pitt, Lindsay et al, Kanis et al) then this would equal a weighted cost per clinical fracture of £1,967. The 35% from Kanis and Pitt is broadly similar to that of 29% calculated from Swedish data.

| Age Range (years) | Updated costs for vertebral fracture (£) | Updated costs for vertebral fracture including home help costs (£) |
|---|---|---|
| 50 – 64 | 1,967 | 3,666 |
| 65 – 74 | 1,967 | 3,666 |
| 75 – 84 | 1,967 | 3,666 |
| 85 + | 1,967 | 3,666 |

Additionally, as previously modelled an ongoing cost of £222 per annum for analgesic drugs.

Note that these costs are lower than those from the Puffer et al paper, which excluding home help costs are over £2,500 for clinical vertebral fracture. These may be seen as conservative as length of stay was assumed to be 6 days, whereas HES data records 10.8 days. These are UK data, and have been attempted to be case-matched to try and ensure that only the costs of the vertebral fractures are included.

It is possible that these costs may be over-estimated were patients with a vertebral fracture also to sustain a hip fracture in the 2-year collection period, as these costs would also be calculated in the model at the time of the hip fracture.

**Additional Costs associated with admission to a nursing home following a vertebral fracture that required hospitalisation.**

We previously assumed that patients would not be forced into nursing home following a vertebral fracture that required hospitalisation. Swedish data provided by John Kanis suggest that the following percentages of patients enter a nursing home following a vertebral fracture that required hospitalisation. If it is assumed that 35% of all clinical vertebral fractures require hospitalisation then the percentage of all clinical vertebral fractures can be inferred.
As we cannot add into formally the costs of nursing home care we have also estimated the additional annual costs of a vertebral fracture that would needed to approximate nursing home costs.

| Age Range (years) | Percentage of vertebral fractures that required hospitalisation that caused the patient to enter nursing home. (Swedish Data) | Percentage of clinical vertebral fractures that caused the patient to enter nursing home. (Swedish Data) | Additional cost (£) per annum to take into account nursing home costs |
|---|---|---|---|
| 50 – 59 | 2 | 0.5 | 126 |
| 60 – 69 | 1 | 0.4 | 84 |
| 70 – 79 | 3 | 1.1 | 262 |
| 80 - 89 | 9 | 3.3 | 794 |

**Wrist fracture.**

This fracture state also includes forearm, ribs, sternum, scapula and clavicle. We have assumed that these bear the same costs as a wrist fracture.

The average length of stay from Hospital Episode Statistics (HES) data for 2003/4 for fractures of forearm is 3.7 days. However this includes younger patients who are likely to have a shorter length of stay. We have thus taken Swedish data in women aged over 50 years, which is 5.4 days for forearm fracture. Fractures at other sites require greater length of stays rib and sternum (6.4 days) scapula (6.3 days) and clavicle (9.7 days), however we have assumed a length of stay of 5.4 days for all 'wrist' fractures.

Given these assumptions we would expect direct medical inpatient stay costs to be 5.4 * £298 = £1609 per hospitalised 'wrist' fracture.

It is estimated that out-patient care costs are 31% that of inpatient costs, which would equal £499.

Thus a hospitalised fracture is expected to cost £2,108 and a non-hospitalised fracture to cost £499. From Kanis and Pitt, it is expected that 25% of wrist fractures are hospitalised, resulting in average costs for a wrist fracture of £901. Additional home help costs of £85 have also been included.

The 25% from Kanis and Pitt is broadly similar to that of 22% calculated from Swedish data for hospitalisation following forearm fracture. The hospitalisation rates following fracture at the ribs, scapula and sternum is lower at 7% and this cost may be slightly over-estimated due to these fracture types being grouped with wrist fractures. However the conservative assumption regarding the length of stay following these fractures will address this to some degree.

| Age Range (years) | Updated costs for wrist fracture (£) | Updated costs for wrist fracture including home help (£) |
|---|---|---|
| 50 – 64 | 901 | 986 |
| 65 - 74 | 901 | 986 |
| 75 - 84 | 901 | 986 |
| 85 + | 901 | 986 |

**Proximal humerus fractures**

This fracture state also includes humerus shaft, tibia and fibula fractures.

The average length of stay from Hospital Episode Statistics (HES) data for 2003/4 for fractures at the shoulder and upper arm is 9.1 days. For fractures of the lower leg this is 10.2 days. These groupings are not appropriate to use since they incorporate lesser fractures, such as scapula and ankle and also because the length of stay is likely to be age-related. We have used Swedish data, which as earlier noted, is likely to be conservative. This estimates a length of stay for 10.6 days for humerus and 13.1 for tibia and fibula fractures, which is associated with costs of £3159 and £3,904 respectively.
We have also assumed that the proportion of inpatient costs associated with out patient care is 10% (the midpoint for hip and vertebral fracture) equalling £316 and £390 respectively.

From Swedish data it is estimated that 32% of proximal humerus fractures and 90% of tibia and fibula fractures are hospitalised

We have used the relative incidence of fracture type by age to calculate costs at each age group. Due to the relatively higher proportion of tibia and fibula fractures at younger ages the weighted cost is higher in the 50 – 59 year age band.

We have assumed an additional £1,143 for home help, equal to that associated with a hip fracture, for tibia and fibula fractures, with a value of £85 for proximal humerus fractures, which are equal to that of a wrist fracture.

| Age Range (years) | Updated costs for a proximal humerus fracture excluding home help costs (£) | Updated costs for a proximal humerus fracture including home help costs (£) |
|---|---|---|
| 50 – 59 | 2,212 | 2,996 |
| 60 – 69 | 1,776 | 2,560 |
| 70 – 79 | 1,660 | 2,444 |
| 80 - 89 | 1,564 | 2,348 |

**Appendix 2b**

**The calculation of costs of fracture using Health Resource Groups (HRGs).**

HRGs detail the costs that are expected to be incurred by a trust when treating a patient with a certain condition. These costs can be modified if the patient has an exceptionally long duration of stay, which is defined as beyond the "trim-point", with additional costs per day after this period. These costs have been centrally calculated, across a large number of NHS trusts and is the methodology recommended by NICE in calculating costs avoided from fewer procedures.

More detail on HRGs can be found at
http://www.nhsia.nhs.uk/def/pages/inform/informish13/informp2.asp

The HRGs used in the estimation of costs are

| | |
|---|---|
| H36 | Closed Pelvis or Lower Limb Fractures >69 or w cc |
| H37 | Closed Pelvis or Lower Limb Fractures <70 w/o cc |
| H39 | Closed Upper Limb Fractures or Dislocations >69 or w cc |
| H40 | Closed Upper Limb Fractures or Dislocations <70 w/o cc |
| H45 | Minor Fractures or Dislocations |
| H82 | Extracapsular Neck of Femur Fracture with Fixation w cc |
| H83 | Extracapsular Neck of Femur Fracture with Fixation w/o cc |
| H84 | Intracapsular Neck of Femur Fracture with Fixation w cc |
| H85 | Intracapsular Neck of Femur Fracture with Fixation w/o cc |
| H86 | Neck of Femur Fracture with Hip Replacement w cc |
| H87 | Neck of Femur Fracture with Hip Replacement w/o cc |
| H88 | Other Neck of Femur Fracture w cc |
| H89 | Other Neck of Femur Fracture w/o cc |
| R15 | Thoracic or Lumbar Spinal Disorders >69 or w cc |
| R16 | Thoracic or Lumbar Spinal Disorders <70 w/o cc |

The costs estimated for a hip, clinical vertebral, wrist and proximal humerus fracture have been provided.

Based on the work previously undertaken it has been assumed that

- The costs for a hip fracture will also incorporate pelvis and other femoral fractures.
- The costs for a wrist fracture will also incorporate rib, scapula, sternum and clavicle fractures.
- The costs for a proximal humerus fracture will also incorporate tibia, fibula and humeral shaft fractures.

1) **Hip Fracture Costs. (Not requiring nursing home admission)**

The average cost from HRG H82-H89 which represent hip fracture is £5,419, with a range of £4,357 to £7,136. The average cost for pelvis and lower limb fracture is dependent on age. For those patients aged over 70 years the cost is £4,582 (H36). For patients under 69 years the cost is £4,582 (H36) if there were complications and £2,417 without (H37).

In the absence of data on the frequency of fractures in relation to HRG code we have assumed that this is the cost of an average hip fracture is £5,419. We have also assumed that an additional 11% costs are incurred from out-patient appointments as indicated by Swedish data, [7] resulting in an average cost of £6,015. We have age-weighted this figure in accordance with data reported by Borgstrom et al.

Some additional costs will be borne for patients who stay longer than the "trim-point". We do not have data on this, but have arbitrarily added £50 on to the cost of a 'hip' fracture, which is approximately 1 additional day's stay beyond the trim point per 3 patients. An additional £93 has been added to each case as a high cost A&E attendance patient. We have assumed an additional £1,568 for home help.

| Age Range (years) | HRG costs for hip fracture excluding home help (£) | HRG costs for hip fracture including Home Help (£) |
|---|---|---|
| 50 – 54 | 4,553 | 5,696 |
| 55 – 59 | 4,553 | 5,696 |
| 60 - 64 | 4,553 | 5,696 |
| 65 – 69 | 5,283 | 6,426 |
| 70 – 74 | 5,607 | 6,750 |
| 75 – 79 | 5,607 | 6,750 |
| 80 – 84 | 5,607 | 6,750 |

Note that these figures are markedly different than those reported in Lawrence that an average hip fracture costs at a Nottingham hospital, which were approximately £12,000 for direct medical costs only.

2) **Additional Costs associated with admission to a nursing home following a hip fracture.**

For the HRG approach we have assumed that the proportions of women entering nursing home originally used are correct, although acknowledge that these may be under-estimates due to women entering a nursing home after initially being discharged to the community.

3) **Vertebral Fracture Costs.**

For patients aged over 69 years we have used the R15 HRG (Thoracic or Lumbar Spinal Disorders >69 or with complications), which is a cost of £2,269. For patients aged below 70 years, we have arbitrarily assumed that 20% have complications (and used R15) and that 80% do not and used R16 (Thoracic or Lumbar Spinal Disorders <70 without complications) at a cost of £1,069. This gives a weighted cost of £1309.

Some additional costs will be borne for patients who stay longer than the "trim-point". We do not have data on this, but have arbitrarily added £50 on to the cost of a vertebral fracture, which is approximately 1 additional day's stay beyond the trim point per 3 patients. An additional £93 has been added to each case as a high cost A&E attendance patient. This equates to costs of £1,452 and £2,412 for hospitalised vertebral fractures for patients aged below 70 years and above 70 years respectively.

Assuming that 35% of clinical vertebral fractures are hospitalised, these equal costs of £508 and £844 on average for all clinical vertebral fractures.

We have assumed additional out-patient costs of 9% of in-patient costs, which are assumed applicable to all patients with a clinical vertebral fracture. This results in costs for patients below 70 years of £639 and costs of £1,061 for patients aged over 69 years.

We have assumed an additional £1,568 for home help. It is assumed that all clinical vertebral fractures will receive medication, at a cost of £222 per annum, as did our previous modelling work.

| Age Range (years) | Updated costs for a clinical vertebral fracture excluding home help (£) | Updated hospital costs for a clinical vertebral fracture including home help (£) |
|---|---|---|
| 50 – 59 | 639 | 2,338 |
| 60 – 69 | 639 | 2,338 |
| 70 – 79 | 1,061 | 2,760 |
| 80 - 89 | 1,061 | 2,760 |

Note that these costs are lower than those from the Puffer et al paper, which excluding home help costs are over £2,500 for clinical vertebral fracture. These may be seen as conservative as length of stay was assumed to be 6 days, whereas HES data records 10.8 days. These are UK data, and have been attempted to be case-matched to try and ensure that only the costs of the vertebral fractures are included.

It is possible that these costs may be over-estimated were patients with a vertebral fracture also to sustain a hip fracture in the 2-year collection period, as these costs would also be calculated in the model at the time of the hip fracture.

4) **Additional Costs associated with admission to a nursing home following a vertebral fracture that required hospitalisation.**

For the HRG approach we have assumed that the proportions of women entering nursing home originally used are correct. Although as it is assumed that no women enter a nursing home following a vertebral fracture these may be under-estimates.

5) **The costs of a 'wrist' fracture.**

For patients aged over 69 years we have used HRG H39 (Closed Upper Limb Fractures or Dislocations >69 or with complications), which has a cost of £2,762. For patients aged below 70 years, we have arbitrarily assumed that 20% have complications (and used H39) and that 80% do not and used H40 (Closed Upper Limb Fractures or Dislocations <70 without complications at a cost of £1,447). This gives a weighted cost of £1,692 for patients under 70 years.

Some additional costs will be borne for patients who stay longer than the "trim-point". We do not have data on this, but have arbitrarily added £50 on to the cost of a wrist fracture, which is approximately 1 additional day's stay beyond the trim point per 3 patients. An additional £61 has been added to each case as a high cost A&E attendance patient. This equates to costs of £1,803 and £2,873 for hospitalised wrist fractures for patients aged below 70 years and above 70 years respectively. Assuming that 25% of wrist fractures are hospitalised, these equal costs of £451 and £718 on average for all wrist fractures.

We have assumed additional out-patient costs of 31% of in-patient costs, which are assumed applicable to all patients with a wrist fracture. This results in costs for patients below 70 years of £1,010 and costs of £1,609 for patients aged over 69 years. We have further assumed an additional £85 for home help.

Rib, clavicle, scapula and sternum fractures have been classified as HRG H45 (Minor Fractures or Dislocations) at a cost of £1,232. We have arbitrarily added £50 on to the cost of a wrist fracture, which is approximately 1 additional day's stay beyond the trim point per 3 patients. An additional £61 has been added to each case as standard A&E attendance patient. This equates to costs of £1,343 per hospitalised fracture.

Using Swedish hospitalisation, incidence and census data, it is assumed that 7% of such fractures are hospitalised [7,8,10], and that 10% of inpatient costs are borne by all fractures as outpatient costs. [7] This equates to £340 per fracture including £85 for home help costs.

The costs at each age band have been weighted to take the proportion of each fracture type into account.

| Age Range (years) | Updated costs for 'wrist' fracture excluding home help costs (£) | Updated costs for 'wrist' fracture including home help costs (£) |
|---|---|---|
| 50 – 54 | 677 | 762 |
| 55 – 59 | 802 | 887 |
| 60 - 64 | 879 | 964 |
| 65 – 69 | 818 | 903 |
| 70 – 74 | 1,176 | 1,261 |
| 75 – 79 | 1,024 | 1,109 |
| 80 + | 919 | 1,004 |

6) **The costs for proximal humerus fractures**

For patients aged over 69 years we have used HRG H39 Closed Upper Limb Fractures or Dislocations >69 or with complications), which has a cost of £2,762. For patients aged below 70 years, we have arbitrarily assumed that 20% have complications (and used H39) and that 80% do not and used H40 (Closed Upper Limb Fractures or Dislocations <70 without complications) at a cost of £1,447. This gives a weighted cost of £1,692. Humerus shaft fractures are assumed to cost the same amount as proximal humerus fractures.

Some additional costs will be borne for patients who stay longer than the "trim-point". We do not have data on this, but have arbitrarily added £50 on to the cost of a proximal humerus fracture, which is approximately 1 additional day's stay beyond the trim point per 3 patients. An additional £61 has been added to each case as a standard A&E attendance patient. This equates to costs of £1,803 and £2,873 for hospitalised proximal humerus fractures for patients aged below 70 years and above 70 years respectively.

Assuming that 32% of proximal humerus fractures are hospitalised, [7,8,10] these equal costs of £577 and £919 on average for proximal humerus fractures in those below 70 years and remaining patients respectively.

We have assumed additional out-patient costs of 10% of in-patient costs, which are assumed applicable to all patients with a proximal humerus fracture. This results in costs for patients below 70 years of £842 and costs of £1,207 for patients aged over 69 years. We have further assumed an additional £85 for home help.

Tibia and fibula fractures have been assumed to cost the same as pelvis and other femoral fractures, which is £4,582 for patients over 69 years or with complications (H36) and £2,850 for patients aged under 70 years without complications (H37).

At all ages an additional £50 has been added for patients staying beyond the trim point. An additional £61 per patient has been included as the cost of a standard A&E admission.

Assuming that 90% of tibia and fibula fractures are hospitalised, [7,8,10] these equal costs of £2,665 when aged below 70 years and £4,224 when aged older than 69 years.

We have assumed additional out-patient costs of 10% of in-patient costs, which are assumed applicable to all patients with a proximal humerus fracture. This results in costs for patients below 70 years of £842 and costs of £1,207 for patients aged over 69 years. We have further assumed an additional £1,143 for home help, equal to that associated with a hip fracture, for tibia and fibula fractures, with a value of £85 for proximal humerus fractures, which are equal to that of a wrist fracture.

The costs at each age band have been weighted to take the proportion of each fracture type into account.

| Age Range (years) | Costs for a proximal humerus fracture excluding home help costs (£) | Costs for a proximal humerus fracture including home help costs (£) |
|---|---|---|
| 50 – 54 | 1,730 | 2,354 |
| 55 – 59 | 1,402 | 1,844 |
| 60 - 64 | 1,198 | 1,527 |
| 65 – 69 | 1,220 | 1,561 |
| 70 – 74 | 1,508 | 1,811 |
| 75 – 79 | 1,450 | 1,711 |
| 80 + | 1,419 | 1,657 |

## References for Appendix 2


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